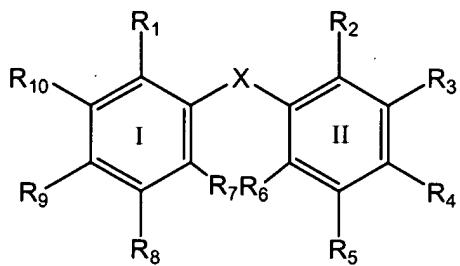


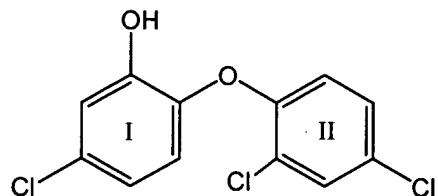
In the claims (Clean version)

9. (Once amended) An antimalarial composition as claimed in claim 7 wherein the inhibitor of fatty acid synthesis used is a hydroxydiphenyl ether of general formula 2 given below wherein the two phenyl rings (I & II) are joined by an oxygen (X=O) atom and either R₁ or R₂ represent a hydroxy (OH) group and the other being a hydrogen atom, respectively, or both being hydroxy groups and other positions (R₃ to R₁₀) of the phenyl rings I and II being substituted in various permutations and combinations by chlorine, bromine or iodine atoms or hydroxy, aldehyde or keto groups or hydrogen atoms or ester group and optionally the two phenyl rings being joined by a sulfur atom (X=S) or by a methylene (X=CH₂) group.



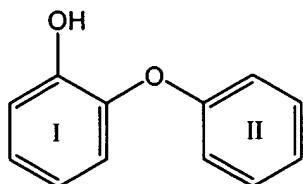
Formula 2

10. (Once amended) An antimalarial composition as claimed in claim 7 wherein the inhibitor of fatty acid synthesis used is a hydroxydiphenyl ether of general formula 2 represented by triclosan [2',4,4'-trichloro-2-hydroxydiphenyl ether which can also be written as 2,4,4''-trichloro-2'-hydroxydiphenyl ether. This is also named as 5-chloro-2-(2,4-dichlorophenoxy)phenol] of formula 1 given below:

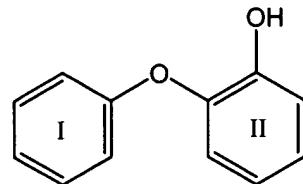


Formula 1

11. (Once amended) An antimalarial composition as claimed in claim 7 wherein the inhibitor of fatty acid synthesis used is a hydroxydiphenyl ether of general formula 2 represented by the compounds of formula 3 and 4 given below:

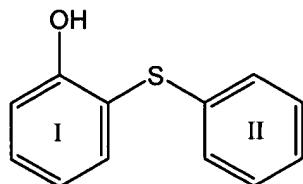


Formula 3

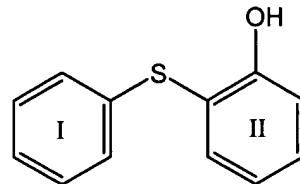


Formula 4

12. (Once amended) An antimalarial composition as claimed in claim 7 wherein the inhibitor of fatty acid synthesis used is a hydroxydiphenyl thioether analogs of general formula 2 represented by the compounds of formulas 5 and 6 given below:

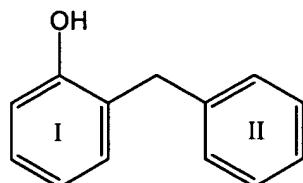


Formula 5

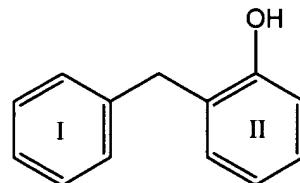


Formula 6

13. (Once amended) An antimalarial composition as claimed in claim 7 wherein the inhibitor of fatty acid synthesis used is a hydroxydiphenyl methane analogs (e.g. Chlorophenes) of general formula 2 represented by the compounds of formulas 7 and 8 given below:



Formulas 7



Formula 8

15. (Once amended) An antimalarial composition as claimed in claim 7 for treating a malarial condition wherein the amount of the fatty acid synthesis inhibitor used is in the dosage range of 0.03 mg/kg to 100 mg/kg of a human or an animal subject for treating a malarial condition.

16. (Once amended) An antimalarial composition as claimed in claim 7 wherein the inhibitor of fatty acid synthesis used is cerulenin.

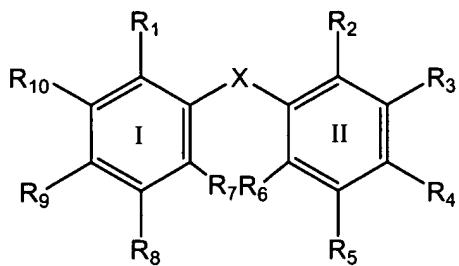
19. (Once amended) An antimalarial drug target as claimed in claim 17 wherein the malarial parasite used is *P. falciparum*.

20. (Once amended) An antimalarial drug target as claimed in claim 17 wherein the malarial parasite used is of human or animal origin.

25. (Once amended) A method of treatment of malaria in a subject, wherein the said method comprising the administration of the composition as claimed in claim 7 to the said subject through a route selected from the group consisting of oral, intramuscular, intradermal, intraperitoneal, intravenous, intra-arterial and subcutaneous.

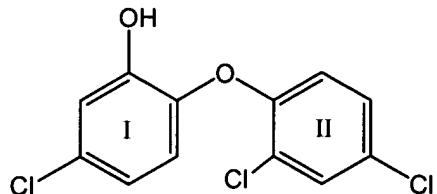
In the claims (Version with markings to show changes made)

9. (Once amended) An antimalarial composition as claimed in claim 7 [1] wherein the inhibitor of fatty acid synthesis used is a hydroxydiphenyl ether of general formula 2 given below wherein the two phenyl rings (I & II) are joined by an oxygen (X=O) atom and either R₁ or R₂ represent a hydroxy (OH) group and the other being a hydrogen atom, respectively, or both being hydroxy groups and other positions (R₃ to R₁₀) of the phenyl rings I and II being substituted in various permutations and combinations by chlorine, bromine or iodine atoms or hydroxy, aldehyde or keto groups or hydrogen atoms or ester group and optionally the two phenyl rings being joined by a sulfur atom (X=S) or by a methylene (X=CH₂) group.



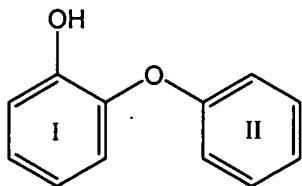
Formula 2

10. (Once amended) An antimalarial composition as claimed in claim 7 [1] wherein the inhibitor of fatty acid synthesis used is a hydroxydiphenyl ether of general formula 2 represented by triclosan [2',4,4'-trichloro-2-hydroxydiphenyl ether which can also be written as 2,4,4"-trichloro-2'-hydroxydiphenyl ether. This is also named as 5-chloro-2-(2,4-dichlorophenoxy)phenol] of formula 1 given below:

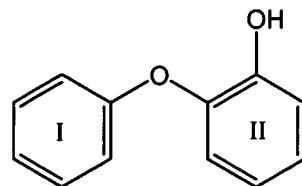


Formula 1

11. (Once amended) An antimalarial composition as claimed in claim 7 [1] wherein the inhibitor of fatty acid synthesis used is a hydroxydiphenyl ether of general formula 2 represented by the compounds of formula 3 and 4 given below:

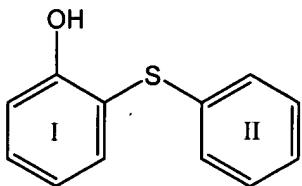


Formula 3

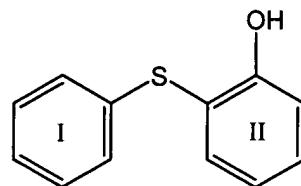


Formula 4

12. (Once amended) An antimalarial composition as claimed in claim 7 [1] wherein the inhibitor of fatty acid synthesis used is a hydroxydiphenyl thioether analogs of general formula 2 represented by the compounds of formulas 5 and 6 given below:

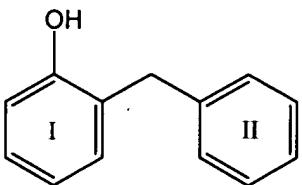


Formula 5

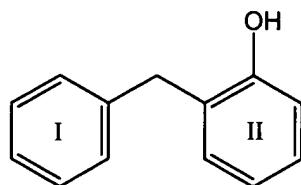


Formula 6

13. (Once amended) An antimalarial composition as claimed in claim 7 [1] wherein the inhibitor of fatty acid synthesis used is a hydroxydiphenyl methane analogs (e.g. Chlorophenes) of general formula 2 represented by the compounds of formulas 7 and 8 given below:



Formulas 7



Formula 8

15. (Once amended) An antimalarial composition as claimed in claim 7 [1] for treating a malarial condition wherein the amount of the fatty acid synthesis inhibitor used is in the dosage range of 0.03 mg/kg to 100 mg/kg of a human or an animal subject for treating a malarial condition.

16. (Once amended) An antimalarial composition as claimed in claim 7 [1] wherein the inhibitor of fatty acid synthesis used is cerulenin.

19. (Once amended) An antimalarial drug target as claimed in claim 17 [10] wherein the malarial parasite used is *P. falciparum*.

20. (Once amended) An antimalarial drug target as claimed in claim 17 [10] wherein the malarial parasite used is of human or animal origin.

25. (Once amended) A method of treatment of malaria in a subject, wherein the said method comprising the administration of the composition as claimed in claim 7 [1] to the said subject through a route selected from the group consisting of oral, intramuscular, intradermal, intraperitoneal, intravenous, intra-arterial and subcutaneous.

Please charge any additional fees that may be associated with this matter to our Deposit Account No. 03-1721.

Respectfully submitted,

Monica R. Gerber
Monica R. Gerber, M.D., Ph.D.
Registration Number 46,724

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Exchange Place
53 State Street
Boston, MA 02109
(617) 248-5000
Dated: May 22, 2003

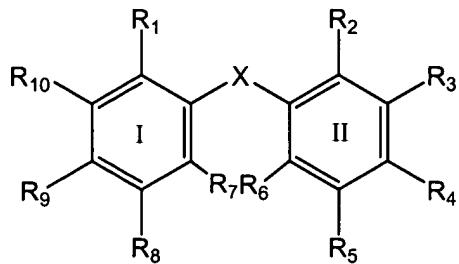
I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner For Patents, P.O. Box 1450, Alexandria, VA 22313

on 05-22-03
Sandra Saccoccia

Appendix A: Clean copy of all claims following entry of this Amendment.

In the claims

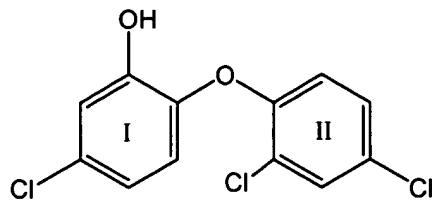
7. An antimalarial composition comprising an inhibitor of fatty acid synthesis of the malarial parasite for treating malaria.
8. An antimalarial composition comprising an inhibitor of fatty acid synthesis or its pharmaceutically acceptable derivatives either alone or in combination with one or more known antimalarials along with a pharmaceutically acceptable adjuvant or a diluent or a carrier.
9. (Once amended) An antimalarial composition as claimed in claim 7 wherein the inhibitor of fatty acid synthesis used is a hydroxydiphenyl ether of general formula 2 given below wherein the two phenyl rings (I & II) are joined by an oxygen (X=O) atom and either R₁ or R₂ represent a hydroxy (OH) group and the other being a hydrogen atom, respectively, or both being hydroxy groups and other positions (R₃ to R₁₀) of the phenyl rings I and II being substituted in various permutations and combinations by chlorine, bromine or iodine atoms or hydroxy, aldehyde or keto groups or hydrogen atoms or ester group and optionally the two phenyl rings being joined by a sulfur atom (X=S) or by a methylene (X=CH₂) group.



Formula 2

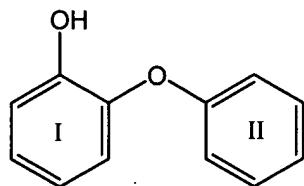
10. (Once amended) An antimalarial composition as claimed in claim 7 wherein the inhibitor of fatty acid synthesis used is a hydroxydiphenyl ether of general formula 2 represented by triclosan [2',4,4'-trichloro-2-hydroxydiphenyl ether which can also be written as 2,4,4"-trichloro-2'-

hydroxydiphenyl ether. This is also named as 5-chloro-2-(2,4-dichlorophenoxy)phenol] of formula 1 given below:

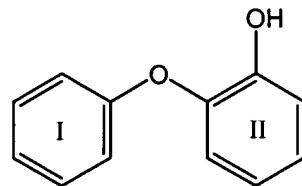


Formula 1

11. (Once amended) An antimalarial composition as claimed in claim 7 wherein the inhibitor of fatty acid synthesis used is a hydroxydiphenyl ether of general formula 2 represented by the compounds of formula 3 and 4 given below:

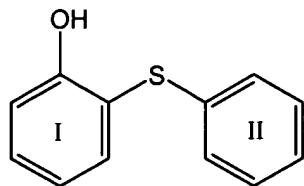


Formula 3

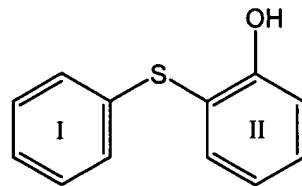


Formula 4

12. (Once amended) An antimalarial composition as claimed in claim 7 wherein the inhibitor of fatty acid synthesis used is a hydroxydiphenyl thioether analogs of general formula 2 represented by the compounds of formulas 5 and 6 given below:

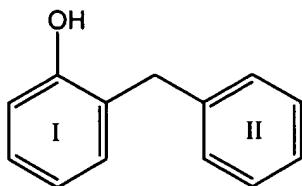


Formula 5

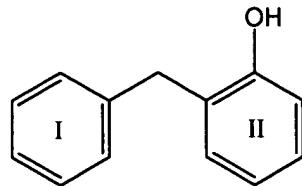


Formula 6

13. (Once amended) An antimalarial composition as claimed in claim 7 wherein the inhibitor of fatty acid synthesis used is a hydroxydiphenyl methane analogs (e.g. Chlorophenes) of general formula 2 represented by the compounds of formulas 7 and 8 given below:



Formulas 7



Formula 8

14. An antimalarial composition consisting of a hydroxydiphenyl ether including triclosan for treating a malarial condition caused by a drug resistant malarial parasite.

15. (Once amended) An antimalarial composition as claimed in claim 7 for treating a malarial condition wherein the amount of the fatty acid synthesis inhibitor used is in the dosage range of 0.03 mg/kg to 100 mg/kg of a human or an animal subject for treating a malarial condition.

16. (Once amended) An antimalarial composition as claimed in claim 7 wherein the inhibitor of fatty acid synthesis used is cerulenin.

17. An antimalarial drug target comprising a component of fatty acid synthesis pathway in a malarial parasite. The components comprise of β -hydroxydecanoyl-ACP dehydrase or β -ketoacyl-ACP synthase I or malonyl-CoA: ACP transacylase or β -ketoacyl-ACP synthase II or β -ketoacyl-ACP reductase or β -ketoacyl-ACP-synthase III or enoyl-ACP reductase or β -hydroxyacyl-ACP dehydrase.

18. An antimalarial drug target comprising a component of fatty acid synthesis pathway where the component is enoyl-ACP reductase activity in a malarial parasite.

19. (Once amended) An antimalarial drug target as claimed in claim 17 wherein the malarial parasite used is *P. falciparum*.

20. (Once amended) An antimalarial drug target as claimed in claim 17 wherein the malarial parasite used is of human or animal origin.

21. A method of inhibiting the growth of human malaria parasite by the use of hydroxydiphenyl ether class of chemicals wherein the said method comprises the steps of:

- a. Examining smears of *in vitro* treated cultures for morphological features of the parasite as an indicator of growth; or
- b. Monitoring the incorporation of [³⁵S] methionine in proteins or [³H]hypoxanthine in nucleic acid as a quantitative indicator of the inhibition of the parasite growth.

22. A method of inhibiting the growth of malaria parasite in an animal, the said method comprising:

- a. Monitoring the extent of inhibition of parasitemia by examining the smears of a blood sample taken from an animal; or
- b. by determining the reduction in the mortality rate of the treated animal vs. untreated animal.

23. A method to determine antimalarial activity of a compound by inhibiting the elongation of fatty acid synthesis in a malaria parasite wherein the said method comprising demonstration of the inhibition of fatty acid synthesis in the cell free fatty acid synthesis system of a malaria parasite by estimating the amount of radioactively labeled malonyl-CoA incorporated into fatty acids or lipids or by analyzing the type of fatty acids synthesized by a chromatographic method.

24. A method to determine the ability of any compound to inhibit the elongation of fatty acid synthesis in malaria parasite by demonstrating the inhibition of fatty acid synthesis in the cell free fatty acid synthesis system of malaria parasite by (a) estimating the incorporation, in the amount of radioactively labeled acetate or other products thereof such as acetyl-CoA, butyryl-CoA, crotonyl-CoA, malonyl-CoA etc. or acetyl-ACP, butyryl-ACP, crotonyl-ACP, malonyl-ACP etc. (ACP; Acyl Carrier Protein) into fatty acids or lipids (b) by analyzing the type of fatty acids synthesized by a chromatographic method.

25. (Once amended) A method of treatment of malaria in a subject, wherein the said method comprising the administration of the composition as claimed in claim 7 to the said subject through a route selected from the group consisting of oral, intramuscular, intradermal, intraperitoneal, intravenous, intra-arterial and subcutaneous.

26. Use of a compound for inhibiting the elongation of fatty acid synthesis in a malaria parasite.

A drug based on the use of a compound for inhibiting the elongation of fatty acid synthesis in malaria parasite.

Use of an inhibitor of fatty acid synthesis or its pharmaceutically acceptable derivative(s) as an antimalarial agent.

27. Use of an inhibitor of fatty acid synthesis or its pharmaceutically acceptable derivatives as an antimalarial agent either alone or in combination with one or more known antimalarials along with a pharmaceutically acceptable adjuvant or a diluent or a carrier.

28. Use of hydroxydiphenyl ether class of chemicals or a pharmaceutically acceptable derivative thereof, as an antimalarial agent.

29. Use of hydroxydiphenyl ether class of chemicals or a pharmaceutically acceptable derivative thereof as antimalarial agents along with a pharmaceutically acceptable adjuvant, or diluent or a carrier.

30. A method for the screening or the designing of drugs using the activity of enoyl-ACP reductase, as a target for treating a malarial infection comprising of the spectrophotometric measurement of its activity using crotonyl-CoA, crotonyl-ACP or other intermediates of fatty acid synthesis as substrates.

31. A method for the screening of drugs using the activity of enoyl-ACP reductase as a target for treating a malarial infection comprising the use of a molecular model of enoyl-ACP reductase of a malarial parasite.

32. An antimalarial drug based on inhibiting the activity of enoyl-ACP reductase in *P. falciparum*.
33. Use of triclosan to treat infection by *P. falciparum*, an apicomplexan parasite.
34. Use of triclosan to treat infection caused by an apicomplexan parasite.
35. Use of a hydroxydiphenyl ether in combination with a biocide for treating a malarial condition.